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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,187	03/05/2001	Christina M. Grozinger	HUV-037.01	3390

25181 7590 04/13/2004

FOLEY HOAG, LLP
PATENT GROUP, WORLD TRADE CENTER WEST
155 SEAPORT BLVD
BOSTON, MA 02110

EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 04/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/800,187	GROZINGER ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,13-24,27,28 and 78-85* is/are pending in the application.

4a) Of the above claim(s) *15 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,13,14,17-24,27,28 and 78-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Sequence alignments; CRF Error Report.

DETAILED ACTION

The amendment file November 3, 2003 amending the specification to insert reference to the sequence identifiers, canceling claims 1, 2, 4-12, 25, 26 and 29-77 and amending claims 3, 13, 14, 17-19, 21, 24, 27 and adding claims 78-85 has been entered.

The Sequence Listing filed November 3, 2003 has been entered.

Claims 3, 13, 14-17, 18-24, 27, 28 and 78-85 are pending. Claims 15, 16 have been previously withdrawn.

Claims 3, 13, 14, 17-24, 27, 28 and 78-85 are under consideration.

Specification

The computer readable form of the Sequence Listing filed November 3, 2003 contains errors. Raw Sequence Listing Error Report is attached to this Office action.

The substitute Sequence listing and CRF are required.

The specification is objected to because it refers to SEQ ID NOs: 1, 3 or 5 as amino acid sequence whereas said sequences are nucleotide sequences (e.g., page 28).

Appropriate correction is required.

Claim Objections

Claims 3, 13, 14, 17-24, 27, 28 and 78-85 are objected to because of the following informalities:

The claims recite "SEQ.ID.NO. X" wherein "SEQ ID NO: X" is customary.

Claim 22 does not end with a period.

Claim 85 recites "polypeptide-having". A hyphen should be deleted.

Appropriate correction is required.

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18, 78, 79 and 81 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 18 has been amended to recite a molecular weight of "131 kD to 208 kD". Applicants indicate support for the amendment on page 4 and page 57. While there is support for 131 kD on page 57, the examiner is unable to locate adequate support in the specification for 208 kD.

Claims 78 and 79 recite a polypeptide sequence having at least 95% homology with SEQID NO:10 and SEQ ID NO:74, respectively. While there is support for a polypeptide sequence having at least 95% homology with SEQ ID NO: 6 (page 28), the examiner is unable to locate adequate support in the specification for 95% homology to fragments of SDQ ID NO:6, including SEQ ID NOs:10 and 74.

Claim 81 recites "at least three-fold deacetylation activity". Applicants indicate support for the claim in Figure 3 and on pages 56-57. While there is support for "two-fold" increase, the examiner is unable to locate adequate support in the specification for "three-fold" increase.

Thus there is no indication that nucleic acids encoding polypeptides having the limitations recited in the claims and discussed above were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims 78, 79 and 84 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 78 and 79 are drawn to a DNA encoding HDAC6 comprising a polypeptide sequence having at least 95% homology with SDQ ID NO:10 and SEQ ID NO:74, respectively.

There is no limitation on the HDAC6 full length amino acid sequence. Furthermore, SEQ ID NO:10 and SEQ ID NO:74 are 73 and 74 amino acids long, respectively, whereas the full length amino acid sequence of HDAC6 of the instant invention (SEQ ID NO:6) is 1215 amino acids long. Thus, SEQ ID NOs: 10 and74 represent about 6% of the full length sequence of SEQ ID NO:6. The recited structural feature of the genus (i.e., comprise a fragment of SEQ ID NO:6 that is SEQ ID NO:10 or SEQ ID NO:74) does not constitute a substantial potion of the genus as the remainder of the structure of a polypeptide with HDAC6 activity is completely undefined. Fragments consisting of 73-74 amino acids of SEQ ID NO:6 by themselves are highly unlikely to have HDAC6 activity and the specification does not define the remaining structural features necessary for members of the genus to be selected.

It is noted that claims 78 and 79 recite not SEQ ID NOs:10 and 74 but the sequences homologous thereto. The homologous sequences as defined on page 20, may not have any identity with SEQ ID NOs: 10 and 74 providing an additional ground for the above consideration.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 84 recites "any cyclic tetrapeptide inhibitors of histone deacetylases". Said genus would comprise a great number of compound both naturally occurring and man

made. The specification teaches no single representative species of the genus of cyclic tetrapeptide inhibitors of histone deacetylases. The specification provides neither information with regard to the structure: function relationship common to all members of the genus nor identifying characteristics that render a cyclic tetrapeptide an inhibitor of histone deacetylase.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 3, 13, 14, 19-24 are 78-85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding HDAC6 of SEQ ID NO:6, including SEQ ID NO:5, does not reasonably provide enablement for a nucleic acid encoding HDAC6 that hybridizes to SEQ ID NO:5 under undefined stringent conditions or encodes a polypeptide that is 85%, 95% or 99% homologous to SEQ ID NO:6 or encodes a polypeptide comprising a sequence that is 95% homologous to SEQ ID NO:10 or SEQ ID NO:74. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,

1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 3 is drawn to a nucleic acid which hybridizes under stringent conditions to a nucleotide sequence designated in SEQ ID NO:5. Since hybridization conditions are not defined, the percent identity to SEQ ID NO:5 is unknown. Claims 13, 14 and 85 recite percent homology that could result in sequences having an unknown percent or no identity with SEQ ID NO:6. Claims 78 and 79 and do not define the HDAC6 structure as discussed above.

The specification does not support the broad scope of the claims which encompass polynucleotides encoding a HDAC6 polypeptide having an unknown identity to SEQ ID NO:6 because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting any HDAC activity and specifically HDAC6 activity; (B) the general tolerance of HDACs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any HDAC6 residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The specification teaches a polynucleotide of SEQ ID NO:5 encoding a HDAC6 of 1215 amino acids (SEQ ID NO:6). The catalytic domains of said HDAC6 are located

at residues 215-287 of SEQ ID NO:6 (SEQ ID NO:10) and residues 610-683 of SEQ ID NO:6 (SEQ ID NO:74). However, a fragment corresponding to SEQ ID NOs:10 or 74 is unlikely to exhibit HDAC6 activity and it constitutes about 6% of the amino acid structure. Despite knowledge in the art to produce mutations in proteins, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to or delete from the known sequence), changes in amino acid residues will result in a desired enzymatic activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited.

Furthermore, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen large numbers of mutated proteins or genes where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

Therefore, one of ordinary skill in the art would require guidance, beyond that provided in the specification, in order to make a polynucleotide encoding a HDAC6 polypeptide that hybridizes to SEQ ID NO:5 under undefined stringent conditions, a polynucleotide encoding a HDAC6 polypeptide that is at least 85%, 95% or 99% homologous to SEQ ID NO:6 or a polynucleotide encoding a HDAC6 polypeptide that comprises SEQ ID NOs:10 or 74 in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 13, 14, 17-24, 27, 28 and 78-85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 13, 14, 17-24, 27, 28 and 78-85 recite "HDAC6 activity". The specification does not define the features that render "an HDAC activity" specifically "HDAC6 activity".

Claims 13, 14, 17-24, 27, 28 and 78-85 recite "% homology". The term homology is not clearly defined by the specification rendering the metes and bound of the claims unascertainable. The specification defines homology as when the equivalent position site is occupied by a "similar amino acid (e.g., similar in steric and/or electronic nature)" (page 20, 1st paragraph). The metes and bounds of "similar" are not clear.

Claims 13, 14, 17, 18-24, 27, 28 and 80-85 are drawn to a nucleic acid encoding an HDAC6 polypeptide wherein said polypeptide sequence has HDAC6 activity. It is presumed that "an HDAC6 polypeptide" has an HDAC6 activity. Further, it is a polypeptide not a sequence thereof that has the activity.

Claim 3 recites "hybridization conditions". The specification def8ens said conditions by non-limiting examples rendering the metes and bounds of the claims unascertainable(pages 14-15).

Claim 18 depends from claim 17 and is drawn to a nucleic acid encoding HDAC6 polypeptide with a molecular weight in the range of 131 kD to 208 kD. Claim17 is drawn

to a nucleic acid encoding a polypeptide of SEQ ID NO:6. While the molecular weight of a polypeptide can vary due to posttranslational modifications, the nucleic acid encoding thereof is the same rendering the difference in scope between claims 17 and 18 unclear.

Claims 80 and 81 recite "activity above background levels". "the background levels" can be obtained with different compositions such as a buffer and a substrate without an enzyme or a buffer without an enzyme and a substrate, for example.

Claim 83 recites "activity that is sensitive". Sensitivity can mean different effects such as inhibition, promotion, etc. and different degrees thereof.

Claim 84 recites "activity that is insensitive". The metes and bounds of said term are defined by neither the specification nor the art.

Claim Rejections - 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 13, 14, 17, 18, 21-23 and 78-85 are rejected under 35 U.S.C. 102(b) as being anticipated by Strom et al. Strom et al. (GenBank accession AJ011972, October 19, 1998) teach a nucleic acid of 4099 bp encoding histone deacetylase-like protein (JM21) of 1215 amino acids having the amino acid sequence that is 100% identical to SEQ ID NO:6. The properties recited in claims 80-84 are inherent to the nucleic acid.

Claim Rejections - 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19-24, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strom et al. in view of Schreiber et al.

The teaching of Strom et al. are outlined above.

Schreiber et al. (WO 97/35990, form PTO-1449, reference BA) teach nucleic acids encoding human histone deacetylases, "*HDx*" genes, and their applications and uses. They teach nucleic acids encoding fusion proteins comprising *HDx* polypeptides (page 3, lines 29-35, claims 34-35). They teach that a nucleic acid can include a transcriptional regulatory sequence and can be included in a vector and cell (page 4, lines 14-21, claims 37-38). Schreiber et al. teach a method of producing an *HDx* polypeptide (claim 39). They teach recombinant transfection systems (claims 42-43).

One of ordinary skill in the art at the time the invention was made would have been motivated to make nucleic acids encoding a fusion protein of an HDAC6 polypeptide, include a regulatory sequence and to put the construct into a cell as well as to prepare a transfection system as required by claims 19-24, 27 and 28 according to the customary uses of nucleic acids in the art that are specifically taught by Schreiber et al. in relation to nucleic acids encoding *HDx* polypeptides. One of ordinary skill in the art

at the time the invention was made would have a reasonable expectation of success because of the high level of knowledge in the field of nucleic acid manipulation and the teachings of Schreiber et al. who successfully applied it to various *HDx* genes.

Response to Arguments

Applicant's arguments filed November 3, 2004 have been fully considered but they are not persuasive.

With regard to the 112,1st written description rejection, Applicants argue that the rejection of claim 3 should be withdrawn in view of the amendment (Remarks, page 14). This is agreed with and amended claim 3 is not rejected for the insufficient written description.

With regard to the 112,1st enablement rejection, Applicants argue that the recitation of the function should obviate the rejection of claim 3 (Remarks, page 14). The rejection above is worded to explain the reasons for which the claims reciting the function lack enablement.

The previous 112, 2nd rejection, is moot in view of the amendment (page 15). However, amended and new claims are rejected under 112, 2nd, for the reasons given above.

With regard to the 102(b) rejection, Applicants argue that "Amino acid 994 of SEQ ID NO:6 is a threonine residue whereas amino acid 994 of the protein sequence of AJ011972 is an isoleucine residue" (page 16). This is incorrect because SEQ ID NO:6 has an isoleucine at position 994. The alignments of GenBank accession AJ011972 and

SEQ ID NO:5 and the sequence encoded thereby and SEQ ID NO:6 are attached to this Office action.

With regard to the 103(a) rejection, Applicants argue that "Strom et al. and Schreiber et al. are devoid of any suggestion, motivation, or guidance to combine each other to make nucleic acids encoding fusion proteins comprising HDAC6 polypeptides or expression vectors, host cells, cell culture and transfection systems for producing recombinant HDA6" (page 17). This is not agreed with for the reasons given above in the rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

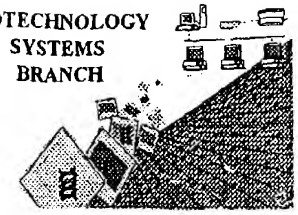
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

April 9, 2004

BIOTECHNOLOGY SYSTEMS BRANCH



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RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/800,187A
Source: 1600
Date Processed by STIC: 11/6/03

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY** or,
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FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 703-308-4212; FAX: 703-308-4221
Effective 12/13/03: **TELEPHONE: 571-272-2510; FAX: 571-273-0221**

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http://www.uspto.gov/web/offices/pac/checker/chkr41note.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
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4. **Federal Express, United Parcel Service, or other delivery service to:** U.S. Patent and Trademark Office, Box Sequence, Room 1B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 10/08/03

1600

RAW SEQUENCE LISTING DATE: 11/06/2003
PATENT APPLICATION: US/09/800,187A TIME: 09:59:06

Input Set : A:\HUV-037.01.st25.txt
Output Set: N:\CRF4\11062003\I800187A.raw

3 <110> APPLICANT: GROZINGER, CHRISTINA M.
4 HASSIG, CHRISTIAN A.
5 SCHREIBER, STUART L.
7 <120> TITLE OF INVENTION: CLASS II HUMAN HISTONE DEACETYLASES, AND USES RELATED
8 THERETO
10 <130> FILE REFERENCE: HUV-037.01
12 <140> CURRENT APPLICATION NUMBER: 09/800,187A
13 <141> CURRENT FILING DATE: 2001-03-05
15 <150> PRIOR APPLICATION NUMBER: 60/186,802
16 <151> PRIOR FILING DATE: 2000-03-03
E--> 18 <160> NUMBER OF SEQ ID NOS: 73 78 (see below)
20 <170> SOFTWARE: PatentIn Ver. 2.1

ERRORED SEQUENCES

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2340 <211> LENGTH: 5
2341 <212> TYPE: PRT
2342 <213> ORGANISM: Artificial Sequence
2344 <220> FEATURE:
2345 <223> OTHER INFORMATION: Description of Artificial Sequence: Consensus
2346 sequence
2348 <220> FEATURE:
2349 <221> NAME/KEY: MOD_RES
2350 <222> LOCATION: (1)
2351 <223> OTHER INFORMATION: Hydrophobic amino acid
2353 <220> FEATURE:
2354 <221> NAME/KEY: MOD_RES
2355 <222> LOCATION: (5)
2356 <223> OTHER INFORMATION: Tyr or His
2358 <400> SEQUENCE: 78
OK> 2359 Xaa Glu Gly Gly Xaa
2360 1 5
E--> 2362 41 delete

Does Not Comply
Corrected Diskette Needed

FYI Use of n and/or Xaa has been detected in the Sequence Listing. Review the Sequence Listing to insure a corresponding explanation is presented in the <220> to <223> fields of each sequence using n or Xaa.

VERIFICATION SUMMARY DATE: 11/06/2003
PATENT APPLICATION: US/09/800,187A TIME: 09:59:07

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M:341 Repeated in SeqNo=7
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L:1598 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:19 after pos.:0
L:1627 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:20 after pos.:0
L:1656 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:21 after pos.:0
L:1680 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:22 after pos.:0
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L:1738 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:24 after pos.:0
L:1757 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:25 after pos.:0
L:2282 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:75 after pos.:0
L:2306 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:76 after pos.:0
L:2335 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:77 after pos.:0
L:2359 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:78 after pos.:0
L:2362 M:332 E: (32) Invalid/Missing Amino Acid Numbering, SEQ ID:78
L:18 M:203 E: No. of Seq. differs, <160> Number Of Sequences:Input (73) Counted (78)

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RESULT 2
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DEFINITION  Homo sapiens mRNA for histone deacetylase-like protein (JM21).
ACCESSION   AJ011972
VERSION     AJ011972.1  GI:3776070
KEYWORDS    histone deacetylase-like protein; jm21 gene.
SOURCE      Homo sapiens.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 4099)
  AUTHORS   Strom,T.M.
  TITLE     Direct Submission
  JOURNAL   Submitted (15-OCT-1998) Strom T.M., Abteilung Medizinische Genetik,
            Goethestr. 29, Muenchen 80336, FRG
REFERENCE   2  (bases 1 to 4099)
  AUTHORS   Strom,T.M., Gutwillinger,N., Nyakatura,G., Hellebrand,H.,
            Drescher,B., Rosenthal,A. and Meindl,A.
  TITLE     Transcription map in Xp11.23
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ORIGIN

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Db       3634 GCCTGGTGTTACTACTGTCAGGCCTATGTCCACCACCAGGCTCTCCTAGATGTGAAGAAC 3693

Qy       3601 ATCGCCCACCAGAACAAGTTTGGGGAGGATATGCCCCACCCACACTAA 3648
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Db       3694 ATCGCCCACCAGAACAAGTTTGGGGAGGATATGCCCCACCCACACTAA 3741
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RESULT 3
AB020708

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LOCUS       AB020708               4078 bp    mRNA    linear   PRI 16-JUN-1999
DEFINITION  Homo sapiens mRNA for KIAA0901 protein, complete cds.
ACCESSION   AB020708
VERSION     AB020708.1  GI:4240290
KEYWORDS    .
SOURCE      Homo sapiens adult male brain cDNA to mRNA, clone_lib:pBluescriptII
            SK plus clone:hk09716.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (sites)
  AUTHORS   Nagase,T., Ishikawa,K., Suyama,M., Kikuno,R., Hirosawa,M.,
            Miyajima,N., Tanaka,A., Kotani,H., Nomura,N. and Ohara,O.
  TITLE     Prediction of the coding sequences of unidentified human genes.
            XII. The complete sequences of 100 new cDNA clones from brain which
            code for large proteins in vitro
  JOURNAL   DNA Res. 5 (6), 355-364 (1998)
  MEDLINE   99156230
REFERENCE   2  (bases 1 to 4078)
  AUTHORS   Ohara,O., Suyama,M., Kikuno,R., Nagase,T. and Ishikawa,K.
  TITLE     Direct Submission
  JOURNAL   Submitted (02-DEC-1998) Osamu Ohara, Kazusa DNA Research Institute,
            Laboratory of DNA Technology; Yana 1532-3, Kisarazu, Chiba
            292-0812, Japan (E-mail:cdnainfo@kazusa.or.jp, Tel:+81-438-52-3913,
            Fax:+81-438-52-3914)
FEATURES             Location/Qualifiers
     source          1. .4078
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /clone="hk09716"
                     /sex="male"
                     /tissue_type="brain"
                     /clone_lib="pBluescriptII SK plus"
                     /dev_stage="adult"
     gene            1. .4078
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GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: June 6, 2003, 14:52:43 ; Search time 18 Seconds
(without alignments)
2799.652 Million cell updates/sec

Title: US-09-800-187-6
Perfect score: 6397
Sequence: 1 MTSTGQDSTTTRQRRSRQNP.....LDVKNIAHQNKFGEDMPHPH 1215

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 112892 seqs, 41476328 residues

Total number of hits satisfying chosen parameters: 112892

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SwissProt_40:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	6397	100.0	1215	1	HDA6_HUMAN	Q9ubn7 homo sapien
2	4667	73.0	1149	1	HDA6_MOUSE	Q9z2v5 mus musculu
3	1347.5	21.1	798	1	YLFN_CAEEL	Q20296 caenorhabdi
4	809	12.6	687	1	HDA1_SCHPO	P56523 schizosacch
5	805.5	12.6	1084	1	HDA4_HUMAN	P56524 homo sapien
6	798	12.5	1080	1	HDA4_CHICK	P83038 gallus gall
7	788	12.3	706	1	HDA1_YEAST	P53973 saccharomyc
8	778.5	12.2	1122	1	HDA5_HUMAN	Q9uql6 homo sapien
9	770	12.0	1113	1	HDA5_MOUSE	Q9z2v6 mus musculu
10	722	11.3	1011	1	HDA9_HUMAN	Q9ukv0 homo sapien
11	457	7.1	359	1	Y130_ARCFU	O30107 archaeoglob
12	419.5	6.6	304	1	Y245_SYNY3	P72702 synechocyst
13	376	5.9	331	1	YB94_METTH	O27262 methanobact
14	362	5.7	343	1	Y535_METJA	Q57955 methanococc
15	345.5	5.4	385	1	ACUC_STAXY	Q56195 staphylococ
16	295.5	4.6	501	1	HDAC_ARATH	O22446 arabidopsis
17	295.5	4.6	513	1	HDAC_MAIZE	P56521 zea mays (m
18	294.5	4.6	433	1	RPD3_YEAST	P32561 saccharomyc
19	289.5	4.5	507	1	HDA2_CAEEL	Q09440 caenorhabdi
20	289	4.5	387	1	ACUC_BACSU	P39067 bacillus su
21	280	4.4	520	1	HDAC_DROME	Q94517 drosophila
22	277.5	4.3	482	1	HDA1_HUMAN	Q13547 homo sapien
23	277	4.3	576	1	HDA1_STRPU	P56518 strongyloce
24	276.5	4.3	482	1	HDA1_MOUSE	O09106 mus musculu
25	273.5	4.3	488	1	HDA2_MOUSE	P70288 mus musculu
26	271	4.2	480	1	HDA1_CHICK	P56517 gallus gall
27	269.5	4.2	480	1	HD12_XENLA	O42227 xenopus lae
28	266.5	4.2	434	1	PHD1_SCHPO	O13298 schizosacch
29	265.5	4.2	488	1	HDA2_HUMAN	Q92769 homo sapien
30	265	4.1	480	1	HD11_XENLA	Q91695 xenopus lae
31	260.5	4.1	341	1	APHA_MYCRA	Q48935 mycoplana r
32	256.5	4.0	310	1	YGLA_SYNP2	P28606 synechococc
33	255.5	4.0	461	1	HDA1_CAEEL	O17695 caenorhabdi
34	252.5	3.9	452	1	HOS2_YEAST	P53096 saccharomyc
35	238.5	3.7	488	1	HDA2_CHICK	P56519 gallus gall
36	227.5	3.6	697	1	HOS3_YEAST	Q02959 saccharomyc
37	225.5	3.5	428	1	HDA3_CHICK	P56520 gallus gall
38	223	3.5	424	1	HDA3_MOUSE	O88895 mus musculu
39	222	3.5	428	1	HDA3_HUMAN	O15379 homo sapien
40	188	2.9	470	1	HOS1_YEAST	Q12214 saccharomyc
41	182.5	2.9	573	1	C114_MOUSE	P19467 mus musculu
42	170.5	2.7	886	1	VGP3_EBVA8	Q07284 epstein-bar
43	160	2.5	542	1	PSGL_ONCMY	P12027 oncorhynchu
44	156.5	2.4	907	1	VGP3_EBV	P03200 epstein-bar
45	151.5	2.4	1509	1	GSR1_HUMAN	Q9nzm4 homo sapien

ALIGNMENTS

```
RESULT 1
HDA6_HUMAN
ID   HDA6_HUMAN      STANDARD;      PRT;  1215 AA.
AC   Q9UBN7;
DT   16-OCT-2001 (Rel. 40, Created)
DT   16-OCT-2001 (Rel. 40, Last sequence update)
DT   16-OCT-2001 (Rel. 40, Last annotation update)
DE   Histone deacetylase 6 (HD6).
GN   HDAC6 OR JM21.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=99238449; PubMed=10220385;
RA   Grozinger C.M., Hassig C.A., Schreiber S.L.;
RT   "Three proteins define a class of human histone deacetylases related
RT   to yeast Hda1p.";
RL   Proc. Natl. Acad. Sci. U.S.A. 96:4868-4873(1999).
RN   [2]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RA   Strom T.M., Gutwillinger N., Nyakatura G., Hellebrand H., Drescher B.,
RA   Rosenthal A., Meindl A.;
RL   Submitted (OCT-1998) to the EMBL/GenBank/DDBJ databases.
CC   -!- FUNCTION: RESPONSIBLE FOR THE DEACETYLATION OF LYSINE RESIDUES ON
CC       THE N-TERMINAL PART OF THE CORE HISTONES (H2A, H2B, H3 AND H4).
CC       HISTONE DEACETYLATION PLAYS AN IMPORTANT ROLE IN TRANSCRIPTIONAL
CC       REGULATION, CELL CYCLE PROGRESSION AND DEVELOPMENTAL EVENTS (BY
CC       SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: Nuclear (By similarity).
CC   -!- SIMILARITY: BELONGS TO THE HISTONE DEACETYLASE / ACUC / APHA
CC       FAMILY. HD SUBFAMILY 2.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC   ---------------------------------------------------------------------
DR   EMBL; AF132609; AAD29048.1; -.
DR   EMBL; AJ011972; CAA09893.1; -.
DR   Genew; HGNC:14064; HDAC6.
DR   MIM; 300272; -.
DR   InterPro; IPR000286; His_deacetylse.
DR   InterPro; IPR001607; Znf_UBP.
DR   Pfam; PF00850; Hist_deacetyl; 2.
DR   Pfam; PF02148; zf-UBP; 1.
DR   PRINTS; PR01270; HDASUPER.
DR   SMART; SM00290; ZnF_UBP; 1.
KW   Hydrolase; Nuclear protein; Repeat.
FT   DOMAIN       87    404       HISTONE DEACETYLASE 1.
FT   DOMAIN      482    800       HISTONE DEACETYLASE 2.
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SQ   SEQUENCE   1215 AA;  131430 MW;  774066633FB11CFA CRC64;

  Query Match           100.0%;  Score 6397;  DB 1;  Length 1215;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 1215;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

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Db          1 MTSTGQDSTTTRQRRSRQNPQSPPQDSSVTSKRNIKKGAVPRSIPNLAEVKKKGKMKKLG 60

Qy         61 QAMEEDLIVGLQGMDLNLEAEALAGTGLVLDEQLNEFHCLWDDSFPEGPERLHAIKEQLI 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 QAMEEDLIVGLQGMDLNLEAEALAGTGLVLDEQLNEFHCLWDDSFPEGPERLHAIKEQLI 120

Qy        121 QEGLLDRCVSFQARFAEKEELMLVHSLEYIDLMETTQYMNEGELRVLADTYDSVYLHPNS 180
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Db        121 QEGLLDRCVSFQARFAEKEELMLVHSLEYIDLMETTQYMNEGELRVLADTYDSVYLHPNS 180

Qy        181 YSCACLASGSVLRLVDAVLGAEIRNGMAIIRPPGHHAQHSLMDGYCMFNHVAVAARYAQQ 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        241 KHRIRRVLIVDWDVHHGQGTQFTFDQDPSVLYFSIHRYEQGRFWPHLKASNWSTTGFGQG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 KHRIRRVLIVDWDVHHGQGTQFTFDQDPSVLYFSIHRYEQGRFWPHLKASNWSTTGFGQG 300

Qy        301 QGYTINVPWNQVGMRDADYIAAFLHVLLPVALEFQPQLVLVAAGFDALQGDPKGEMAATP 360
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Db        301 QGYTINVPWNQVGMRDADYIAAFLHVLLPVALEFQPQLVLVAAGFDALQGDPKGEMAATP 360

Qy        361 AGFAQLTHLLMGLAGGKLILSLEGGYNLRALAEGVSASLHTLLGDPCPMLESPGAPCRSA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 AGFAQLTHLLMGLAGGKLILSLEGGYNLRALAEGVSASLHTLLGDPCPMLESPGAPCRSA 420

Qy        421 QASVSCALEALEPFWEVLVRSTETVERDNMEEDNVEESEEEGPWEPPVLPILTWPVLQSR 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 QASVSCALEALEPFWEVLVRSTETVERDNMEEDNVEESEEEGPWEPPVLPILTWPVLQSR 480

Qy        481 TGLVYDQNMMNHCNLWDSHHPEVPQRILRIMCRLEELGLAGRCLTLTPRPATEAELLTCH 540
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Db        481 TGLVYDQNMMNHCNLWDSHHPEVPQRILRIMCRLEELGLAGRCLTLTPRPATEAELLTCH 540

Qy        541 SAEYVGHLRATEKMKTRELHRESSNFDSIYICPSTFACAQLATGAACRLVEAVLSGEVLN 600
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Db        541 SAEYVGHLRATEKMKTRELHRESSNFDSIYICPSTFACAQLATGAACRLVEAVLSGEVLN 600

Qy        601 GAAVVRPPGHHAEQDAACGFCFFNSVAVAARHAQTISGHALRILIVDWDVHHGNGTQHMF 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        661 EDDPSVLYVSLHRYDHGTFFPMGDEGASSQIGRAAGTGFTVNVAWNGPRMGDADYLAAWH 720
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Qy        721 RLVLPIAYEFNPELVLVSAGFDAARGDPLGGCQVSPEGYAHLTHLLMGLASGRIILILEG 780
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Qy        781 GYNLTSISESMAACTRSLLGDPPPLLTLPRPPLSGALASITETIQVHRRYWRSLRVMKVE 840
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Qy        841 DREGPSSSKLVTKKAPQPAKPRLAERMTTREKKVLEAGMGKVTSASFGEESTPGQTNSET 900
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Qy        901 AVVALTQDQPSEAATGGATLAQTISEAAIGGAMLGQTTSEEAVGGATPDQTTSEETVGGA 960
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Db        901 AVVALTQDQPSEAATGGATLAQTISEAAIGGAMLGQTTSEEAVGGATPDQTTSEETVGGA 960

Qy        961 ILDQTTSEDAVGGATLGQTTSEEAVGGATLAQTISEAAMEGATLDQTTSEEAPGGTELIQ 1020
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Db        961 ILDQTTSEDAVGGATLGQTTSEEAVGGATLAQTISEAAMEGATLDQTTSEEAPGGTELIQ 1020

Qy       1021 TPLASSTDHQTPPTSPVQGTTPQISPSTLIGSLRTLELGSESQGASESQAPGEENLLGEA 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 TPLASSTDHQTPPTSPVQGTTPQISPSTLIGSLRTLELGSESQGASESQAPGEENLLGEA 1080

Qy       1081 AGGQDMADSMLMQGSRGLTDQAIFYAVTPLPWCPHLVAVCPIPAAGLDVTQPCGDCGTIQ 1140
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Db       1081 AGGQDMADSMLMQGSRGLTDQAIFYAVTPLPWCPHLVAVCPIPAAGLDVTQPCGDCGTIQ 1140

Qy       1141 ENWVCLSCYQVYCGRYINGHMLQHHGNSGHPLVLSYIDLSAWCYYCQAYVHHQALLDVKN 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 ENWVCLSCYQVYCGRYINGHMLQHHGNSGHPLVLSYIDLSAWCYYCQAYVHHQALLDVKN 1200

Qy       1201 IAHQNKFGEDMPHPH 1215
              |||||||||||||||
Db       1201 IAHQNKFGEDMPHPH 1215


RESULT 2
HDA6_MOUSE
ID   HDA6_MOUSE     STANDARD;      PRT;  1149 AA.
AC   Q9Z2V5;
DT   16-OCT-2001 (Rel. 40, Created)
DT   16-OCT-2001 (Rel. 40, Last sequence update)
DT   16-OCT-2001 (Rel. 40, Last annotation update)
DE   Histone deacetylase 6 (HD6) (Histone deacetylase mHDA2).
GN   HDAC6.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=C57BL/6J; TISSUE=Fetal;
RX   MEDLINE=99107904; PubMed=9891014;
RA   Verdel A., Khochbin S.;
RT   "Identification of a new family of higher eukaryotic histone
RT   deacetylases. Coordinate expression of differentiation-dependent
RT   chromatin modifiers.";
RL   J. Biol. Chem. 274:2440-2445(1999).
CC   -!- FUNCTION: RESPONSIBLE FOR THE DEACETYLATION OF LYSINE RESIDUES ON
CC       THE N-TERMINAL PART OF THE CORE HISTONES (H2A, H2B, H3 AND H4).
CC       HISTONE DEACETYLATION PLAYS AN IMPORTANT ROLE IN TRANSCRIPTIONAL
CC       REGULATION, CELL CYCLE PROGRESSION AND DEVELOPMENTAL EVENTS (BY
CC       SIMILARITY).
CC   -!- SUBCELLULAR LOCATION: Nuclear (By similarity).
CC   -!- SIMILARITY: BELONGS TO THE HISTONE DEACETYLASE / ACUC / APHA
CC       FAMILY. HD SUBFAMILY 2.
CC   ----------------------------------------------------------------------
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CC   ----------------------------------------------------------------------
DR   EMBL; AF006603; AAD09835.2; -.
DR   MGD; MGI:1333752; Hdac6.
DR   InterPro; IPR000286; His_deacetylse.
DR   InterPro; IPR001607; Znf_UBP.
DR   Pfam; PF00850; Hist_deacetyl; 2.
DR   Pfam; PF02148; zf-UBP; 1.
DR   PRINTS; PR01270; HDASUPER.
DR   SMART; SM00290; ZnF_UBP; 1.
KW   Hydrolase; Nuclear protein; Repeat.
FT   DOMAIN       87    403       HISTONE DEACETYLASE 1.
FT   DOMAIN      481    799       HISTONE DEACETYLASE 2.
FT   DOMAIN      455    460       POLY-GLU.
SQ   SEQUENCE   1149 AA;  125703 MW;  2B98CDB228CE0D1D CRC64;

  Query Match           73.0%;  Score 4667;  DB 1;  Length 1149;
  Best Local Similarity  74.4%;  Pred. No. 2.7e-286;
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